

The invention features a nucleic acid molecule which includes a fragment of at least 150 (300, 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1800, 2000, 2250, 2500, 2750, 3000, 3250, 3500, 3750, or 4000) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, the nucleotide

~~sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, or a complement thereof.~~

Replace the paragraph beginning at page 9, line 34 with the following amended paragraph:

The invention also features a nucleic acid molecule that hybridizes to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:25, ~~the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_, or a complement thereof,~~ under conditions of incubation at 45°C in 6.0X SSC followed by washing in 0.2X SSC/0.1% SDS at 65°C.

Replace the paragraph beginning at page 10, line 9 with the following amended paragraph:

In an embodiment, a PYRIN-2 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 10, line 11 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2 ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 10, line 14 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:1 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 10, line 28 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-2 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2 ~~or the amino acid sequence encoded by the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-2 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:2 (e.g., about amino acid residues 1-93 of SEQ ID NO:2); an isolated PYRIN-2 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:2 (e.g., about amino acids 146-169 of SEQ ID NO:2); an isolated PYRIN-2 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:2 (e.g., about amino acids 146-169 of SEQ ID NO:2); an isolated PYRIN-2 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the LRR domain of SEQ ID NO:2 (e.g., about amino acids 196-449 of SEQ ID NO:2); and an isolated PYRIN-2 protein

having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to one or more of the leucine rich repeats of SEQ ID NO:2 (e.g., about amino acids residues 196-223, 250-278, 280-307, 308-335, 337-364, 365-392, 394-421, and 422-449 of SEQ ID NO:2).

Replace the paragraph beginning at page 11, line 10 with the following amended paragraph:

In an embodiment, a PYRIN-3 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:3, SEQ ID NO:23, or SEQ ID NO:25, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 11, line 13 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:4, or SEQ ID NO:24, ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 11, line 16 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:24, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:3, or SEQ ID NO:25, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 11, line 31 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:4; ~~or SEQ ID NO:24; or the amino acid sequence encoded by the cDNA of ATCC~~ \_\_\_\_\_; and an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:4 or SEQ ID NO:24 (e.g., about amino acid residues 1-83 of SEQ ID NO:4 or SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:24 (e.g., about amino acids 150-466 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:24 (e.g., about amino acids 150-172 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif II domain of SEQ ID NO:24 (e.g., about amino acids 179-209 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 2 domain of SEQ ID NO:24 (e.g., about amino acids 213-236 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 3a domain of SEQ ID NO:24 (e.g., about amino acids 257-282 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif V domain of SEQ ID NO:24 (e.g., about amino acids 333-353 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VI domain of SEQ ID NO:24 (e.g., about amino acids 421-436 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VII domain of SEQ ID NO:24 (e.g., about amino acids 447-466 of SEQ ID NO:24); an isolated PYRIN-3 protein having an amino acid sequence

that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the LRR domain of SEQ ID NO:24 (e.g., about amino acids 637-947 of SEQ ID NO:24); and an isolated PYRIN-3 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to one or more of the leucine rich repeats of SEQ ID NO:24 (e.g., about amino acids residues 637-664, 722-749, 750-776, 806-833, 835-862, 863-890, 892-919, and 920-947 of SEQ ID NO:24).

Replace the paragraph beginning at page 12, line 29 with the following amended paragraph:

In an embodiment, a PYRIN-5 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:5 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 12, line 31 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:6 ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 12, line 34 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:6, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:5 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 13, line 12 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:6 ~~or the amino acid sequence encoded by the cDNA of ATCC~~ \_\_\_\_\_; an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:6 (e.g., about amino acid residues 1-91 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:6 (e.g., about amino acids 188-506 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:6 (e.g., about amino acids 188-211 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif II domain of SEQ ID NO:6 (e.g., about amino acids 218-248 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 2 domain of SEQ ID NO:6 (e.g., about amino acids 252-275 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 3a domain of SEQ ID NO:6 (e.g., about amino acids 295-320 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif V domain of SEQ ID NO:6 (e.g., about amino acids 371-391 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VI domain of SEQ ID NO:6 (e.g., about amino acids 461-476 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VII domain of SEQ ID NO:6 (e.g., about amino acids 487-506 of SEQ ID NO:6); an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or

98% identical to the LRR domain of SEQ ID NO:6 (e.g., about amino acids 688-1056 of SEQ ID NO:6); and an isolated PYRIN-5 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to one or more of the leucine rich repeats of SEQ ID NO:6 (e.g., about amino acids residues 688-715, 744-771, 773-800, 801-828, 830-857, 858-885, 887-914, 915-942, 944-971, 972-1000, 1001-1028, and 1029-1056 of SEQ ID NO:6).

Replace the paragraph beginning at page 14, line 10 with the following amended paragraph:

In an embodiment, a PYRIN-6 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:7 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 14, line 12 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:8 ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 14, line 15 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:8, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:7 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 14, line 29 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-6 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino



acid sequence of SEQ ID NO:8 ~~or the amino acid sequence encoded by the cDNA of ATCC \_\_\_\_\_~~; and an isolated PYRIN-6 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:8 (e.g., about amino acid residues 1-91 of SEQ ID NO:8).

Replace the paragraph beginning at page 15, line 1 with the following amended paragraph:

In an embodiment, a PYRIN-7 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 15, line 4 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:10, or SEQ ID NO:13, ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 15, line 7 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:10 or SEQ ID NO:13, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 15, line 22 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:10; ~~or SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acid residues 1-52 of SEQ ID NO:10 or 1-98 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 167-480 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 167-190 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif II domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 197-227 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 2 domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 231-254 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 3a domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 270-295 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif V domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 346-366 of SEQ ID NO:13); an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VI domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 435-450 of SEQ ID NO:13); and an isolated PYRIN-7 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to

the Motif VII domain of SEQ ID NO:10 or SEQ ID NO:13 (e.g., about amino acids 461-480 of SEQ ID NO:13).

Replace the paragraph beginning at page 16, line 16 with the following amended paragraph:

In an embodiment, a PYRIN-8 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 16, line 19 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:15; or SEQ ID NO:18; ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 16, line 22 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:15 or SEQ ID NO:18, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17, ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 17, line 1 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:15; or SEQ ID NO:18; ~~or the amino acid sequence encoded by the~~

cDNA of ATCC \_\_\_\_\_; an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acid residues 1-65 of SEQ ID NO:15 or 1-107 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 212-528 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 212-234 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif II domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 241-272 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 2 domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 276-299 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 3a domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 320-345 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif V domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 396-416 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VI domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 483-498 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VII domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 509-528 of SEQ ID NO:18); an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the LRR domain of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids 712-1052 of SEQ ID NO:18); and an isolated PYRIN-8 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or

98% identical to one or more of the leucine rich repeats of SEQ ID NO:15 or SEQ ID NO:18 (e.g., about amino acids residues 712-739, 741-768, 769-796, 798-825, 826-853, 855-882, 883-910, 912-939, 940-967, 969-996, 997-1024, and 1026-1052 of SEQ ID NO:18).

Replace the paragraph beginning at page 18, line 3 with the following amended paragraph:

In an embodiment, a PYRIN-10 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:19 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 18, line 6 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:20 ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 18, line 9 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:20, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:19 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 18, line 23 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-10 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:20 ~~or the amino acid sequence encoded by the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-10 protein having an amino acid sequence that is at least about 65%,

preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:20 (e.g., about amino acid residues 41-112 of SEQ ID NO:20); an isolated PYRIN-10 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the LRR domain of SEQ ID NO:20 (e.g., about amino acids 210-440 of SEQ ID NO:20); and an isolated PYRIN-10 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to one or more of the leucine rich repeats of SEQ ID NO:20 (e.g., about amino acids residues 210-237, 267-294, 299-326, 356-383, 385-412, and 413-440 of SEQ ID NO:20).

Replace the paragraph beginning at page 19, line 1 with the following amended paragraph:

In an embodiment, a PYRIN-11 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:21 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 19, line 4 with the following amended paragraph:

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:22 ~~or the polypeptide encoded by the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 19, line 7 with the following amended paragraph:

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:22, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule consisting of SEQ ID NO:21 ~~or the nucleotide sequence of the cDNA of ATCC \_\_\_\_\_~~ under stringent conditions.

Replace the paragraph beginning at page 19, line 21 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:22 ~~or the amino acid sequence encoded by the cDNA of ATCC~~       ; an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the pyrin domain of SEQ ID NO:22 (e.g., about amino acid residues 1-102 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the NBS domain of SEQ ID NO:22 (e.g., about amino acids 177-494 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 1a domain of SEQ ID NO:22 (e.g., about amino acids 177-200 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif II domain of SEQ ID NO:22 (e.g., about amino acids 207-237 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 2 domain of SEQ ID NO:22 (e.g., about amino acids 241-264 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the kinase 3a domain of SEQ ID NO:22 (e.g., about amino acids 285-310 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif V domain of SEQ ID NO:22 (e.g., about amino acids 361-381 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VI domain of SEQ ID NO:22 (e.g., about amino acids 449-464 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to the Motif VII domain of SEQ ID NO:22 (e.g., about amino acids 475-494 of SEQ ID NO:22); an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or

98% identical to the LRR domain of SEQ ID NO:22 (e.g., about amino acids 615-813 of SEQ ID NO:22); and an isolated PYRIN-11 protein having an amino acid sequence that is at least about 65%, preferably 75%, 85%, 95%, or 98% identical to one or more of the leucine rich repeats of SEQ ID NO:22 (e.g., about amino acids residues 615-642, 644-671, 672-699, 701-728, 729-756, 758-785, and 786-813 of SEQ ID NO:22).

Replace the paragraph beginning at page 20, line 19 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:1 ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:1; an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:1; an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a encoding portion of SEQ ID NO:1; an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:1 or one or more leucine rich repeat encoding portions of SEQ ID NO:1; and an isolated PYRIN-2 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_~~.



Replace the paragraph beginning at page 21, line 1 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:3, SEQ ID NO:23, ~~or~~ SEQ ID NO:25, ~~or the cDNA of~~ ATCC \_\_\_\_\_; an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:3, SEQ ID NO:23, or SEQ ID NO:25; an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:23 or SEQ ID NO:25; an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a, Motif II, kinase 2, kinase 3a region, Motif V, Motif VI, or Motif VII encoding portion of SEQ ID NO:23 or SEQ ID NO:25; an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:23 or SEQ ID NO:25 or one or more leucine rich repeat encoding portions of SEQ ID NO:23 or SEQ ID NO:25; and an isolated PYRIN-3 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:3, SEQ ID NO:23, ~~or~~ SEQ ID NO:25; ~~or the non-coding strand of the cDNA of~~ ATCC \_\_\_\_\_.

Replace the paragraph beginning at page 21, line 22 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:5 ~~or the cDNA of~~ ATCC \_\_\_\_\_; an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65%

preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:5; an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:5; an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a, Motif II, kinase 2, kinase 3a region, Motif V, Motif VI, or Motif VII encoding portion of SEQ ID NO:5; an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:5 or one or more leucine rich repeat encoding portions of SEQ ID NO:5; and an isolated PYRIN-5 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:5 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 22, line 4 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-6 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:7 ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-6 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:7; and an isolated PYRIN-6 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:7 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 22, line 13 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-7 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12; ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-7 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12; an isolated PYRIN-7 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12; an isolated PYRIN-7 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a, Motif II, kinase 2, kinase 3a region, Motif V, Motif VI, or Motif VII encoding portion of SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12; and an isolated PYRIN-7 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:12 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 22, line 30 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17; ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17; an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at

least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17; an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a, Motif II, kinase 2, kinase 3a region, Motif V, Motif VI, or Motif VII encoding portion of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17; an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17 or one or more leucine rich repeat encoding portions of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17; and an isolated PYRIN-8 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:17 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 23, line 16 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-10 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:19 ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-10 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:19; an isolated PYRIN-10 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:19 or one or more leucine rich repeat encoding portions of SEQ ID NO:19; and an isolated PYRIN-10 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:19 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 23, line 29 with the following amended paragraph:

Also within the invention are: an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:21 ~~or the cDNA of ATCC \_\_\_\_\_~~; an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the pyrin domain encoding portion of SEQ ID NO:21; an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the NBS domain encoding portion of SEQ ID NO:21; an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the kinase 1a, Motif II, kinase 2, kinase 3a region, Motif V, Motif VI, or Motif VII encoding portion of SEQ ID NO:21; an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 65% preferably 75%, 85%, or 95% identical to the LRR domain encoding portion of SEQ ID NO:21 or one or more leucine rich repeat encoding portions of SEQ ID NO:21; and an isolated PYRIN-11 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:21 ~~or the non-coding strand of the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 24, line 16 with the following amended paragraph:

Another embodiment of the invention features PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecules which specifically detect PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecules, relative to nucleic acid molecules encoding other members of the PYRIN/NBS/LRR superfamily. For example, in one embodiment, a PYRIN-2, PYRIN-3,

PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or a complement thereof.~~ In another embodiment, the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecule is at least 300 (350, 400, 450, 500, 550, 600, 650, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1800, 2000, 2250, 2500, 2750, 3000, 3250, 3500, 3750, or 4000) nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or a complement thereof.~~ In another embodiment, an isolated PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecule comprises the pyrin domain encoding portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, or a complement thereof. In another embodiment, an isolated PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecule comprises the NBS domain encoding portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, or a complement thereof. In another embodiment, an isolated PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecule

comprises the LRR domain encoding portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, or a complement thereof. In yet another embodiment, the invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid.

Delete the paragraph beginning at page 44, line 2, which starts with "A plasmid containing".

Delete the paragraph beginning at page 44, line 9, which starts with "A plasmid containing".

Delete the paragraph beginning at page 45, line 4, which starts with "A plasmid containing".

Delete the paragraph beginning at page 45, line 11, which starts with "A plasmid containing".

Delete the paragraph beginning at page 45, line 18, which starts with "A plasmid containing".

Delete the paragraph beginning at page 45, line 25, which starts with "A plasmid containing".

Delete the paragraph beginning at page 45, line 32, which starts with "A plasmid containing".

Delete the paragraph beginning at page 46, line 3, which starts with "A plasmid containing".

Replace the paragraph beginning at page 48, line 24 with the following amended paragraph:

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_,~~ or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, ~~or SEQ ID NO:25, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~ as a hybridization probe, PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleic acid molecules can be isolated using standard hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

Replace the paragraph beginning at page 49, line 14 with the following amended paragraph:

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID



NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_,~~ or a portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Replace the paragraph beginning at page 49, line 25 with the following amended paragraph:

Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11. The nucleotide sequence determined from the cloning of the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 gene allows for the generation of probes and primers designed for use in identifying and/or cloning PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 homologues in other cell types, e.g., from other tissues, as well as PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 homologues and orthologs from other mammals. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the~~

~~eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, or of a naturally occurring mutant of one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, or SEQ ID NO:25; the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, or the eDNA of ATCC \_\_\_\_\_.~~

Replace the paragraph beginning at page 50, line 30 with the following amended paragraph:

A nucleic acid fragment encoding a "biologically active portion" of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, or SEQ ID NO:25; ~~the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, the eDNA of ATCC \_\_\_\_\_, or the eDNA of ATCC \_\_\_\_\_~~ which encodes a polypeptide having a PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 biological activity, expressing the encoded portion of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 protein (e.g., by recombinant expression in vitro) and assessing the activity of the encoded portion of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11.

Replace the paragraph beginning at page 51, line 7 with the following amended paragraph:

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, ~~or~~ SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~ due to degeneracy of the genetic code and thus encode the same PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, ~~or~~ SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~.

Replace the paragraph beginning at page 51, line 21 with the following amended paragraph:

In addition to the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 nucleotide sequences shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, ~~or~~ SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 may exist within a population (e.g., the human population). Such genetic polymorphism in the PYRIN-2, PYRIN-3,

Replace the paragraph beginning at page 52, line 19 with the following amended paragraph:

[illegible]

Replace the paragraph beginning at page 53, line 6 with the following amended paragraph:

In addition to naturally-occurring allelic variants of the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, or SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_,~~ thereby leading to changes in the amino acid sequence of the encoded protein without altering the functional ability of the protein. For example, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 protein without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11, proteins of various species are predicted to be particularly unamenable to alteration.

Replace the paragraph beginning at page 53, line 32 with the following amended paragraph:

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 proteins that contain changes in amino acid residues that are not essential for activity. Such PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ

ID NO:8, SEQ ID NO:10, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24 and yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24. An isolated nucleic acid molecule encoding a PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 protein having a sequence which differs from that of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, or SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_,~~ can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, ~~or SEQ ID NO:25, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~) such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. Thus, for example, 1%, 2%, 3%, 5%, or 10% of the amino acids can be replaced by conservative substitution. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side

chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

Replace the paragraph beginning at page 86, line 3 with the following amended paragraph:

A transgenic animal of the invention can be created by introducing PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 cDNA sequence, e.g., that of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, or SEQ ID NO:25, ~~the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, the cDNA of ATCC \_\_\_\_\_, or the cDNA of ATCC \_\_\_\_\_~~ can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homolog or

ortholog of the human PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 gene, such as a mouse PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 gene, can be isolated based on hybridization to the human PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 transgene to direct expression of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 transgene in its genome and/or expression of PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 can further be bred to other transgenic animals carrying other transgenes.